REMARKS

Claims 27-29, 35-41, and 43-67 are pending in the present application.

As a preliminary matter, the specification has been amended to update the status of the applications in the section entitled "CROSS REFERENCE TO RELATED APPLICATIONS."

I. Formal Drawings for Figures 4 and 5A

The corrected drawings (Figures 4 and 5A) submitted on May 1, 2003 were disapproved as allegedly introducing new matter. Applicants submit herewith formal drawings for Figures 4 and 5A, which contain subject matter that is identical to the as-filed drawings. No substantive changes have been made. Accordingly, the present rejection is moot.

II. The Specification Contains No Hyperlinks

The Office Action asserts that the specification is objected to because it allegedly contains an embedded hyperlink and/or other form of browser-executable code. The substitute specification filed on October 17, 2002, and subsequently entered into the record (see, Office Action dated January 15, 2003, at page 2), however, contains no hyperlinks or other forms of browser-executable code. The Office Action specifically refers to "ncbi.nlm.nih.gov/Omim/." This term, however, is merely the name of the web site and is purposefully missing the "http://www." prefix required for it to serve as a hyperlink. Thus, the specification in its current form contains no hyperlinks. Accordingly, Applicants respectfully request that the objection to the specification be withdrawn.

III. The Claimed Invention Is Useful

Claims 27-29, 35-41, and 43-67 are rejected under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. The Office Action asserts that the claims "do not sufficiently distinguish over naturally [sic] nucleic acids..." Applicants traverse the rejection and respectfully request reconsideration thereof because the claims are recite statutory subject matter.

The Office Action suggest amending the claims to recite "isolated" or "purified" to distinguish the claimed subject matter from the naturally occurring products. Each of the claims

27-29, 35-41, and 43-67 recite an "oligonucleotide." Applicants are unaware of any "naturally occurring" oligonucleotides that comprise the same recited features as Applicants' claimed "oligonucleotides." Indeed, the naturally occurring nucleic acid molecules that comprise the molecular interaction sites are molecules much larger than "oligonucleotides." Further, Applicants are not merely "isolating" or "purifying" molecules that are found in nature. Upon a showing that such claimed compounds are found in nature, Applicants will entertain the Office Action's suggestion to further amend the claims. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §101 be withdrawn.

IV. The Claimed Invention Is Novel

A. The Molecular Biology of the Cell Reference

Claims 35-40, 43-57, and 59-67 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by The Molecular Biology of The Cell, Third Edition, 1994, page 466 (hereinafter, the "Molecular Biology reference"). The Office Action asserts that the polyA tail of the mRNA molecule shown at page 466 of the Molecular Biology reference is a molecular interaction site and, thus, anticipates the cited claims. Applicants traverse the rejection and respectfully request reconsideration because the Molecular Biology reference does not teach every feature recited in the claims.

The standard for anticipation under § 102(b) is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984).

Each of the rejected independent claims recites an "**oligonucleotide** comprising a molecular interaction site..." (emphasis added). Page 466 of the Molecular Biology reference does not teach any oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site. Rather, the nucleic acid molecule that contains the polyA tail depicted on page 466 of the Molecular Biology reference is an mRNA. An mRNA molecule is not an oligonucleotide.

Thus, the Molecular Biology reference does not teach every feature recited in the claims. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

B. The Biochemistry Reference

Claims 27, 35-38, 41, 43-55, and 58-67 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Biochemistry, Third Edition, 1993, pages 817 and 818 (hereinafter, the "Biochemistry reference"). The Office Action asserts that the tRNA molecule depicted on page 818 contains a molecular interaction site for RNase P and, thus, anticipates the cited claims. Applicants traverse the rejection and respectfully request reconsideration because the Biochemistry reference does not teach every feature recited in the claims.

Each of the rejected independent claims recites an "**oligonucleotide** comprising a molecular interaction site..." (emphasis added). Page 818 of the Biochemistry reference does not teach any oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site. Rather, the nucleic acid molecule that contains the RNase P binding site is an entire tRNA molecule. An entire tRNA molecule is not an oligonucleotide. Indeed, the molecular interaction sites which is present within the claimed oligonucleotides is present in the RNA of a selected organism. Although the RNA that is within the selected organism can be a tRNA, the oligonucleotide is not a tRNA molecule.

Thus, Biochemistry reference does not teach every feature recited in the claims. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

V. The Claimed Invention Is Supported by Ample Written Description

A. The Claims Recite No New Matter

Claims 27-29, 35-41, and 43-67 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants traverse the rejection

and respectfully request reconsideration because the specification provides ample written description supporting the claimed inventions.

The Office Action asserts that the specification does not adequately describe an oligonucleotide that comprises a molecular interaction site that is present in an RNA that does not comprise the iron response element or the 3' untranslated region of histone RNA. Applicants' specification, however, acknowledges that both the iron response element and the 3' untranslated region of histone RNA are known molecular interactions sites. Indeed, Applicants teach in Example 3 that the analysis shown "describes the use of this known structure to validate the strategy and methods described herein." Thus, Applicants used both the iron response element and the 3' untranslated region of histone RNA to validate the methods described in the specification. Applicants validation of the methods described in the present application resulted in identifying molecular interaction sites in, for example, ornithine decarboxylase and vimentin, as well as others. Thus, Applicants clearly intended not to claim either the iron response element or the 3' untranslated region of histone RNA, which were clearly identified in the present application to be known. Applicants also teach at, for example, page 2 of the specification that the process of RNA maturation, transport, intracellular localization and translation are rich in RNA recognition sites that provide good opportunities for drug binding. Thus, modulation of translation is but one alternative function of a molecular interaction site.

In addition, it is established law that a specification which describes the claims as filed necessarily describes those embodiments following limiting amendments. *In re Johnson*, 558194 U.S.P.Q. 187 (C.C.P.A. 1977). Indeed, MPEP §2173.05(i) states:

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims.

Thus, because both the iron response element and the 3' untranslated region of histone RNA are positively recited in the present specification and are alternative elements, along with other molecular interaction sites such as ornithine decarboxylase and vimentin, they may be explicitly excluded in the claims. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

B. Claims 27-29, 35-41, and 43-67

Claims 27-29, 35-41, and 43-67 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants traverse the rejection and respectfully request reconsideration because the specification provides ample written description supporting the claimed inventions.

As a preliminary matter, the Office Action acknowledges that the present specification provides adequate written description for: 1) iron response element in the 5' untranslated region of ferritin RNA and in 3' untranslated region of transferring receptor mRNA; 2) 3' untranslated region of histone mRNA; 3) 3' untranslated region of vimentin mRNA; 4) 5' and 3' untranslated regions of ornithine decarboxylase mRNA; 5) 5' and 3' untranslated regions of interleukin-2 mRNA; and 6) 5' and 3' untranslated regions of interleukin-4 mRNA. The Office Action, however, asserts that only the iron response element can be considered a molecular interaction site because it is the only one of those listed that has been demonstrated to modulate the expression of the RNA. The Office Action further asserts that the since the specification only provides sufficient written description of an oligonucleotide comprising the iron response element as the molecular interaction site, the present specification fails to provide sufficient written description for the breadth of the recited claims.

A patent Applicant's disclosure, which contains a teaching of how to make and use the invention, **must** be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *In re Marzocchi*, 439 F.2d 220, 223-224 (CCPA 1971); *In re Brauna* 34 USPQ2d 1437, 1441 (Fed. Cir.1995). Indeed, the Office Action has provided no reasoning nor evidence to suggest that the molecular interaction sites identified in, for example, histone, vimentin, ornithine decarboxylase, interleukin-2, or interleukin-4 mRNA cannot serve as a binding site for at least one molecule that when bound to the molecular interaction site modulates the expression of the RNA. Indeed, each of these molecular interaction sites contains ample secondary structure to serves as binding sites for other molecules. No evidence to the contrary has been presented in the Office Action. Further, any assertion by the Patent Office that

an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974). Thus, Applicants' specification provides numerous representative species.

Claims 35-41 and 43-67 recite an oligonucleotide product that comprises a molecular interaction site, wherein the molecular interaction site is identified by the recited method. As such, these claims should be treated as product-by-process claims. Section 2163 of the MPEP teaches:

> [D]isclosure of only a method of making the invention and the function may not be sufficient to support a product claim other than a product-by-process claim.

(citation omitted). Thus, because Applicants' recited method is supported by ample written description, product-by-process claims 35-41 and 43-67 are sufficiently described to show that Applicants' were, in fact, in possession of that which is claimed.

Nevertheless, claims 27-29, 35-41, and 43-67 are supported by ample written description. The written description requirement for a claim drawn to a genus may be satisfied through sufficient description of: 1) a representative number of species by actual reduction to practice, 2) reduction to drawings, or 3) disclosure of relevant, identifying characteristics (i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus). Under this standard, Applicants have provided sufficient written description of the claimed invention.

Applicants' specification discloses a representative number of species. Applicants' specification teaches an actual reduction to practice of the following representative species, in addition to iron response element and histone RNA used to validate their methodology: 1) vimentin RNA (see, Example 4), 2) ornithine decarboxylase (see, Example 6), 3) interleukin-2 (see, Example 7), and 4) interleukin-4 (see, Example 8). The Office Action fails to provide **any** reasoning or evidence to support the position that such representative number of species is in any way inadequate.

Applicants' specification also teaches sufficient identifying characteristics of the claimed invention. Referring to claim 27, for example, the claimed oligonucleotide comprises a molecular interaction site. The specification is replete with the underlying characteristics of a molecular interaction site. Another recited identifying characteristic is that the molecular interaction site is present in prokaryotic RNA. Another recited identifying characteristic is that the molecular interaction site is present in at least one additional prokaryotic RNA. In addition, another recited identifying characteristic is that the molecular interaction site serves as a binding site for at least one molecule that when bound to the molecular interaction site modulates the expression of the prokaryotic RNA. These recited identifying characteristics are sufficient to show that Applicants were in possession of the claimed genus. The Office Action fails to provide **any** reasoning or evidence to support the position that such identifying characteristics are in any way inadequate.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, as allegedly failing to provide sufficient written description be withdrawn.

VI. The Claimed Invention Is Sufficiently Enabled

Claims 27-29 are rejected under 35 U.S.C. §112, first paragraph as allegedly failing to provide an enabling disclosure. The Office Action mistakenly asserts that it would require undue experimentation for one skilled in the art to determine whether the molecular interaction site can modulate the expression of prokaryotic RNA but not modulate translation of prokaryotic RNA. Applicants traverse the rejection and respectfully request reconsideration because one skilled in the art would be able to practice the claimed invention without being required to perform undue experimentation.

The Office Action asserts that the specification fails to provide guidance showing that the binding of a molecule to a molecular interaction site of a prokaryotic RNA "only can modulate the expression of said prokaryotic RNA but can not modulate translation of said RNA" (see, Office Action at page 17). Claim 27, however, does not recite that the binding of a molecule to a molecular interaction site "**only**" can modulate the expression of the prokaryotic

RNA while not modulating translation of the RNA. The only functional language recited in claim 27 is that the "molecular interaction site serves as a binding site for at least one molecule that when bound to said molecular interaction site modulates the expression of said prokaryotic RNA" and that "the binding of said molecule to said molecular interaction site does not modulate translation of said RNA." One skilled in the art desiring to determine whether: 1) a "molecular interaction site serves as a binding site for at least one molecule that when bound to said molecular interaction site modulates the expression of said prokaryotic RNA"; and 2) "the binding of said molecule to said molecular interaction site does not modulate translation of said RNA" need only perform routine experimentation. Nowhere does the Office Action suggest, let alone support with evidence, that such testing is anything but routine. Indeed, RNA expression assays and RNA translation assays have been widely known to and used by the skilled artisan for years. Further, experiments to determine the rate of transcription, RNA maturation, RNA transport, and intracellular RNA localization, each of which can modulate the expression of the prokaryotic RNA.

Thus, there is no reason to believe that one skilled in the art would be required to perform any amount of undue experimentation to make and use the claimed invention. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn.

VII. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 665-6914 if there are any questions regarding Applicants' claimed invention.

Respectfully submitted,

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Enclosures: Figures 4 and 5A